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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte RALPH MOCIKAT

Appeal 2010-007342
Application 10/716,580
Technology Center 1600

Before CAROL A. SPIEGEL, JEFFREY N. FREDMAN, and STEPHEN WALSH, *Administrative Patent Judges*.

WALSH, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

This is an appeal under 35 U.S.C. § 134(a) involving claims to a vector for the expression of immunoglobulin-cytokine fusion proteins in malignant B cells. The Patent Examiner rejected the claims as failing to

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

comply with the written description requirement, as anticipated, and as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

Claims 1-5, 7-9, and 11-17 are on appeal. Claims 1 and 12 are representative and read as follows:

1. A vector for the expression of immunoglobulin-cytokine fusion proteins in malignant B cells, comprising the following components operably linked to each other

(a) a continuous region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the k intron;

(b) at least one DNA sequence encoding a constant region of an immunoglobulin or a part of the constant region;

(c) a DNA sequence encoding a cytokine; and

(d) a marker gene which is selectable in eukaryotic B cells and contains a functional enhancer region.

12. The vector according to claim 1, wherein the DNA sequence of (b) encodes the constant region of a mouse, rat, goat, horse or sheep immunoglobulin.

The Examiner rejected the claims as follows:

- claims 1-5, 7-9, and 11-17 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement;
- claims 1-5, 7-9, 11, and 13-17, and 29 under 35 U.S.C. §102(e) as anticipated by Polack,[2] as evidenced by Mucke;[3]
- claims 1-5, 7-9, 11-13, and 15-17 under 35 U.S.C. § 103(a) as unpatentable over Polack, Levy[4], and Gillies,[5] as evidenced by Mucke;

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[2] US Patent No. 6,521,449 B1 issued to Axel Polack, et al., Feb. 18, 2003.
[3] S. Mücke, et al., *Suitability of Epstein-Barr virus-based episomal vectors for expression of cytokine genes in human lymphoma cells,* 4 GENE THERAPY, 82-92 (1997).
[4] US Patent No. 6,099,846 issued to Ronald Levy, et al., Aug. 8, 2000.

• claims 1-5, 7-9, 11-17 under 35 U.S.C. § 103(a) as unpatentable over Mucke, Polack, and Mocikat.[6]

Claims 2-5, 7-9, and 11-17 have not been argued separately and therefore stand or fall with claim 1 in each rejection. 37 C.F.R. § 41.37(c)(1)(vii).

WRITTEN DESCRIPTION

The Issue

The Examiner's position is that the claims are drawn to multiple genera of vectors. (Ans. 3). The Examiner found that apart from the disclosure of one exemplary vector in the Specification and the vectors disclosed in the prior art, a skilled artisan would have "to guess at the multiple vector components from which to pick and choose in order to construct vectors encompassed by the instant claims." (*Id.* at 5). According to the Examiner, "the instant claims and Specification do nothing more than suggest various vector components in the form of generic lists or as a laundry list of potential components that one of ordinary skill in the art could piece together to obtain possession of the claimed genus of vectors." (*Id.*, citing *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916 (Fed. Cir. 2004) and *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009)).

The Examiner also found that the prior art of record "shows that the large size of the *k* locus makes it exceedingly difficult to determine which homologous intron segments structurally constitute the claimed region of "at

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[5] US Patent No. 5,650,150 issued to Stephen D. Gillies, Jul 22, 1997.
[6] R. Mocikat, et al., *Unaltered immunoglobulin expression in hybridoma cells modified by targeting of the heavy chain locus with an integration vector*, 84 IMMUNOLOGY 159-163 (1995).

least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the *k* intron." (*Id.* at 6). The Examiner found that "[i]n the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genera of vectors to establish that Appellant was in possession of the vectors in their full scope." (*Id.* at 7).

Appellant contends that, in contrast to *Rochester* or *Kubin*, at the time their application was filed all of the "components of the claimed vector-- μ or *k* intron sequences, immunoglobulin constant region sequences, cytokine sequences, selectable marker sequences, and enhancer sequences, were well known and available to a person of ordinary skill in the art." (App. Br. 6, 8). Appellant asserts that the disclosure provides sufficient detail such that a skilled artisan would reasonably conclude that the inventor had possession of the claimed invention at the time of filing. (*Id.*).

The issue with respect to this rejection is whether the Examiner established that a person of ordinary skill in the art would understand that Appellant was in possession of the claimed invention.

Findings of Fact

1. The Examiner does not dispute that the μ or *k* intron sequences, immunoglobulin constant region sequences, cytokine sequences, selectable marker sequences, and enhancer sequences of the claimed invention were well known to a person of ordinary skill in the art at the time of the invention. (*See* Ans. 4-5, 18).

2. The Specification states, "The homologous sequence contained in said vector must have a length of at least 1.5 kb to achieve a homologous recombination event at all." (Spec. 10).

Principles of Law

When an Applicant claims a class, the Applicant "must describe that class in order to meet the description requirement of the statute." *In re Lukach*, 442 F.2d 967, 968 (CCPA 1971). "The adequate written description requirement . . . serves 'to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him; how the specification accomplishes this is not material.'" *In re Alton*, 76 F.3d 1168, 1172 (Fed. Cir. 1996) (citation omitted). The amount of description needed to meet the requirement can vary with the scientific and technologic knowledge already in existence. *Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005). "It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention." *Id.* at 1359.

It is well settled that "claims in an application are to be given their broadest reasonable interpretation consistent with the specification and that claim language should be read in light of the specification as it would be interpreted by one of ordinary skill in the art." *In re Sneed*, 710 F.2d 1544, 1548 (Fed. Cir. 1983).

Analysis

A. Claim Interpretation

We turn to the Specification for clarification as to the meaning and scope of the claim phrase "homologous to an at least 1.5 kb segment of the μ intron or the k intron" recited in claim 1. *See Sneed*, 710 F.2d at 1548. The Examiner's position is that "[s]imply knowing the nucleic acid code of a μ intron or k intron is not sufficient to describe a representative number of

species or to adequately show possession when the claim limitations, as written, recite ...a region which is homologous to an at least 1.5 kb segment of the μ intron or the *k* intron." (Ans. 6). According to the Examiner, a skilled artisan would require knowing something more about the structure of the homologous regions required for the vector to be apprised that Appellant was in possession of a generic homologous region of a genus of *k* introns. (*Id.*). However, the Specification describes the homologous sequence contained in claimed vector as "hav[ing] a length of at least 1.5 kb *to achieve a homologous recombination event* at all." (Spec. 10, emphasis added).

In light of the Specification, we interpret the claim phrase "homologous to an at least 1.5 kb segment of the μ intron or the *k* intron" broadly as referring to any homology to an at least 1.5 kb segment of the μ intron or the *k* intron, both of which are known sequences (FF-1), that is sufficient to achieve homologous recombination. There is no evidence to support the Examiner's finding that a person of ordinary skill in the art would have needed more examples to recognize that Appellant had possession of homologous regions.

B. Appellant's Possession of the Claimed Invention

We agree with Appellant that a skilled artisan at the time of filing would have understood that Appellant was in possession of the claimed invention as the components of the claimed vector were known in the art. (FF-1). This fact distinguishes this situation from the facts of *Rochester* and *Kubin*, for the reasons asserted by Appellant. (*See* App. Br. 7-8). As the Federal Circuit explained in *Capon*, "[t]he 'written description' requirement must be applied in the context of the particular invention and the state of the

knowledge." *See Capon*, 418 F.3d at 1358. A re-description of what was already known in the art is not necessary to satisfy this requirement. *Id.* at 1357. Moreover, "every permutation within a generally operable invention" does not have to be described. *Id.* at 1359. The written description examination guidelines in the MANUAL OF PATENT EXAMINING PROCEDURE apply those principles: "[g]enerally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement. Information which is well known in the art need not be described in detail in the specification." (MPEP § 2163 II.A.2).

Here, similar to *Capon*, the invention is not in discovering the DNA sequences which are the components of the claimed vector, for that is in the prior art, but instead in the novel combination, i.e., operable linkage, of the DNA sequences to achieve a novel result, i.e., a vector for the expression of immunoglobulin-cytokine fusion proteins in malignant B cells. There are likely a variety of ways to describe that invention, but how the Specification accomplishes the description is not material. *Alton*, 76 F.3d at 1172. The rejection demands one kind of description (more examples), rather than the kind of description the Specification gave. That requirement has not been shown to be supportable under the applicable precedent and the application of the precedent by the written description examination guidelines in the MPEP.

ANTICIPATION

The Issue

The Examiner's position is that Polack disclosed each limitation of the instant claims, including "a combination of kappa E3′ and kappa Ei

enhancers ... exceed[ing] the 'at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the *k* intron,'" recited in instant claim 1. (Ans. 8-10). The Examiner also found that Polack disclosed BC219-TNFα vector integrated into BL60 cells capable of expressing TNFα. (*Id.* at 9; compare with instant claim 29). The Examiner referenced Mucke to demonstrate the inherent features of Polack's vector. (*Id.* at 9). Specifically, the Examiner found that Mucke's BC219 vector illustrated Polack's vector in detail and demonstrated that the kappa E3′ and the kappa Ei of Polack's vector provided a combined length of approximately 2.64 kb. (*Id.*).

Appellant contends that "neither Polack nor Mucke provides the limitation of 'a continuous region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the *k* intron'...." (App. Br. 9). Appellant asserts that "Polack describes the combined use of two enhancer k intron elements, which provide a combined length of over 1.5 kb but each is less than 1.5 kb...." (*Id.*). According to Appellant (Reply Br. 5-6) the claim phrase "continuous region" should be interpreted as requiring "an uninterrupted or unbroken polynucleotide sequence having a defined minimal length as well as a sequence homology" and not as comprising "a multiplicity of segments," as the Examiner asserted (Ans. 24).

The issues with respect to the anticipation rejection are:

whether the claimed "continuous region" should be interpreted as requiring a single, "uninterrupted or unbroken polynucleotide sequence having a defined minimal length as well as a sequence homology"; and

whether Polack disclosed "a continuous region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the *k* intron."

Additional Findings of Fact

3. We agree with the Examiner's explicit findings regarding the scope and content of Polack and Mucke. (*See* Ans. 8-10).

4. Merriam-Webster Online Dictionary defines "continuous" as "marked by *uninterrupted extension in space, time, or sequence*." (Reply Br. 5, Ex. A).

Principle of Law

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987).

Analysis

The Specification does not define "continuous." Appellant asserts that the plain meaning of the word is "an uninterrupted or unbroken polynucleotide sequence having a defined minimal length as well as a sequence homology." (Reply Br. 5). However, the plain meaning of the term "continuous" is not so limiting. (*See* FF-2). The plain meaning of the term is consistent with the Examiner's reasoning (Ans. 21) that two enhancer regions located adjacent to each other in a vector, as illustrated in Mucke, "will innately be continuous with one another," i.e., in an uninterrupted extension in space, time, or sequence. We agree with the Examiner that the placement of "continuous" "does not limit the homologous region to being continuous segments from the μ intron or the k intron that are each individually at least 1.5 kb in length." (*Id.*). The Specification does not require a narrower interpretation. Therefore, we

interpret the phrase "continuous region" to broadly include a region comprising either one required gene segment or more than one of the required gene segments positioned in a continuous, i.e., uninterrupted sequence with each other. It is the Applicants' burden to precisely define the invention, not the PTO's. *In re Morris*, 127 F.3d 1048, 1056 (Fed. Cir. 1997).

Giving the phrase "continuous region" its broadest reasonable interpretation, it is reasonable to interpret the phrase to include Polack and Mucke's vector region comprising the kappa E3′ and the kappa Ei. While these are two separate enhancer elements, they are positioned adjacent to each other in a continuous manner.

For these reasons, we do find that Appellant has not established that the Examiner erred in determining that Polack and Mucke disclosed a vector comprising "a continuous region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the k intron." Accordingly, we affirm the anticipation rejection.

OBVIOUSNESS

The Issue

The Examiner's position is that Polack and Mucke disclosed all of the limitations of claim 1. (Ans. 11, 14-15). For the rejection over Polack, Mucke, Levy and Gillies, the Examiner also found that Levy and Gillies taught the limitations of the dependent claims that were not disclosed by Polack and Mucke. (*Id.* at 12). According to the Examiner, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the prior art elements according to known methods to yield predictable results. (*Id.* at 13).

For the rejection over Polack, Mucke and Mocikat, the Examiner found that Mocikat disclosed the limitations of the dependent claims that were not disclosed by Polack and Mucke. (*Id.* at 15). In particular, regarding instant claim 12, the Examiner found that Mocikat disclosed a vector for homologous recombination at the immunoglobulin (Ig) locus comprising a murine IgH locus including a 5′ homology flank. (*Id.*). The Examiner also found that Mocikat's vector comprised a 2.3 kb fragment from the mouse μ intron. (*Id.*). According to the Examiner, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the prior art elements according to known methods to yield predictable results. (*Id.* at 16). In particular, the Examiner reasoned that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to create a vector capable of expressing an immunoglobulin-cytokine fusion protein in malignant B cells, as taught by Polack and Mucke, using at least one DNA sequence encoding part of a mouse immunoglobulin constant region, such as the 5′ homology flank from the IgH locus taught by Mocikat, with predictable results. (*Id.* at 16-17). According to the Examiner, combining or substituting "at least one DNA sequence encoding a part of a mouse constant region in the vector construct for the human constant region [would have provided] predictable results because of similarities in mouse and human constant regions, which are old and well known in the art." (*Id.* at 17).

Appellant contends that claims are not obvious over the combination including Polack and Mucke for the same reasons asserted regarding anticipation rejection, i.e., Polack and Mucke fail to disclose "a continuous

region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the *k* intron," as recited in claim 1. (App. Br. 10).

Regarding the rejection over Polack, Mucke and Mocikat, Appellant further contends that Mocikat's use of a 2.3 kb fragment of the mouse μ intron sequence in the recombination vector does not supplement the missing claim limitation. (*Id.* at 10-11). According to Appellant, there would not be any motivation to combine Polack and Mocikat "because of fundamental differences in the purpose and mechanism of action between expression vectors (*e.g.*, the Polack vector) and integration vectors (*e.g.*, the Mocikat vector)...." (*Id.* at 11). Additionally, Appellant asserts that replacing Polack's expression vector enhancers with the 2.3 kb intron sequence of Mocikat "would completely defeat the purpose of enhancing/promoting expression." (*Id.*).

The issues with respect to these rejections are:

whether the combination of Polack and Mucke taught or suggested "a continuous region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the *k* intron;" and

whether the combination of Polack, Mucke and Mocikat taught or suggested a vector according to instant claim 1, wherein at least one DNA sequence encodes the constant region of a mouse immunoglobulin.

Additional Finding of Fact

5. We agree with the Examiner's explicit findings regarding the scope and content of Levy, Gillies, and Mocikat. (*See* Ans. 10-17).

Principle of Law

"The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR Int'l. Co. v. Teleflex Inc.,* 550 U.S. 398, 416 (2007).

Analysis

To the extent that Appellant asserts that Polack and Mucke did not disclose "a continuous region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the *k* intron," we remain unpersuaded for the reasons discussed regarding the anticipation rejection.

Further, we disagree with Appellant that the Examiner's combination of Polack, Mucke and Mocikat was improper. (*See* App. Br. 10-11). Appellant's arguments are directed to the replacement of enhancers in Polack's expression vector with the 2.3 kb intron sequence of Mocikat as a means of supplementing the asserted "missing claim limitation" of "a continuous region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the *k* intron." (*Id.*). However, as discussed, this claim limitation is met by the disclosures of Polack and Mucke. As the Examiner explained, "[t]he Mocikat reference was cited against the limitations of claim 12, which … recites that the DNA sequence … encodes the constant region of a mouse [immunoglobulin]." (Ans. 25). For this limitation, the Examiner's combination only involved substituting at least one DNA sequence encoding a part of a mouse constant region in the vector construct for the human constant region. (*Id.* at 17). By explaining that mouse and human constant regions share similarities that were well known in the art the Examiner provided sound reasoning that this substitution would

have been obvious to a skilled artisan at the time of the invention, and would have provided predictable results.

For these reasons, we find that Examiner's rejection involved combining familiar elements according to known methods to yield a predictable, i.e., disclosed, result. *See KSR Int'l,* 550 U.S. at 416-17.

CONCLUSIONS OF LAW

The Examiner did not establish that a person of ordinary skill in the art would require additional descriptions of the recited vector or its components to credit Appellant with possession of the claimed invention.

Polack disclosed "a continuous region of at least 1.5 kb which is homologous to an at least 1.5 kb segment of the μ intron or the *k* intron."

A person of ordinary skill in the art at the time the invention was made would have found it obvious to combine the known elements of the prior art to yield the claimed invention.

SUMMARY

We reverse the rejection of claims 1-5, 7-9, and 11-17 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement;

we affirm the rejection of claims 1-5, 7-9, 11, and 13-17, and 29 under 35 U.S.C. §102(e) as anticipated by Polack, as evidenced by Mucke;

we affirm the rejection of claims 1-5, 7-9, 11-13, and 15-17 under 35 U.S.C. § 103(a) as unpatentable over Polack, Levy, and Gillies, as evidenced by Mucke;

we affirm the rejection of claims 1-5, 7-9, 11-17 under 35 U.S.C. § 103(a) as unpatentable over Mucke, Polack, and Mocikat.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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